REMARKS

Claims 15 and 31-35 are pending. No claim amendments are made herein.

Claims 15 and 31-35 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kimura et al. in view of Postma et al. (Office Action, page 2)

The rejection stated that the amount of TA-270 used in the experiment of the Declaration as filed on July 30, 2008 was 10 times more than the amount of theophylline. The rejection also stated that TA-270 does not decrease eosinophilia only, as it is disclosed to decrease total inflammatory cell accumulation in the lung, this includes not only eosinophils but also macrophages and neutrophils.

The Applicant further conducted an additional experiment, using a LPS-induced model of COPD, to demonstrate the unexpected therapeutic effects on COPD of TA-270 of the claimed invention and to rebut the above assertions. The results are shown as Experiment 1 in attached Declaration.

The administration doses between TA-270 and theophylline were different in Experiment 2 of the Declaration as filed on July 30, 2008. Theophylline has been known that it has both bronchodilator and anti-airway inflammatory action through its non-specific PDE (phosphodiesterase) inhibitor. However theophylline has a central nervous stimulating effect and a myocardial stimulating effect as side effects and there is not so much of a difference between its efficacious dose and toxic dose. Therefore, in Experiment 2, almost the maximum dose of theophylline was used without side effects such as convulsion or death, etc. Although the unexpected effects of TA-270 were shown sufficiently in Experiment 2, an additional experiment was conducted showing the effects on COPD in an *equal dose between TA-270 and theophylline*.

In this experiment, TA-270 and theophylline were intra-tracheally administered to COPD mice induced by lipopolysaccharide (LPS) and evaluated on its efficacy and prolonged effect. This COPD model, particularly the LPS-Induced Model of COPD, was reported in the attached journal article on p.L10, Am J Physiol Lung Cell Mol Physiol (295: L1–L15, 2008). The LPS-Induced Model of COPD is known in the art and intra-tracheal administration was chosen to avoid the side-effects of theophylline.

According to the results of Experiment 1 in the attached Declaration, total cell, macrophages, lymphocyte and neutrophil counts in BALF of the positive group were significantly increased through the intra-tracheal dose (ITD) of LPS as compared to the normal group. Eosinophils was not detected in any group including to normal, positive and test compound groups.

TA-270 showed the significant inhibitory effects on the infiltration of inflammatory cells into airway by intra-tracheal dose at dose of *10 μg/kg*. Additionally, TA-270 showed the significant effect by intra-tracheal dose at 24 hours prior to administration of LPS and this long-acting effect meant the possibility that TA-270 was effective in an inhalation dose once a day in COPD patients. These effects were not thought to be related to allergic reaction through eosinophils, because eosinophils could not be detected in this COPD model. On the other hand, *theophylline did not show any inhibitory effects at a similar dose of TA-270 in any dose timings.*

Therefore, as shown in Experiment 2 of the Declaration as filed on July 30, 2008 and Experiment 1 of the attached Declaration, TA-270 has the unexpected and superior effect than existing medicine for COPD, theophylline, in two COPD animal models. TA-270 improved the residual volume, had a stronger inhibitory effect on the infiltration of inflammatory cells than theophylline and showed the long-acting effects in COPD model.

Accordingly, Kimura et al. in view of Postma et al. does not in fact make claims 15 and 31-35 *prima facie* obvious. Thus this rejection should overcome based on the empirical evidence submitted. It is respectfully requested that the rejection be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105.

Dated: September 28, 2010

Respectfully submitted,

Customer No. 21874

Electronic signature: /James E. Armstrong, IV/
James E. Armstrong, IV
Registration No.: 42,266
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(202) 478-7375
Attorneys/Agents For Applicant

Attachments: Declaration (6 pages); and

Am J Physiol Lung Cell Mol Physiol (295: L1–L15, 2008) (16 pages)